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BALSA, An Integrated Software Environment for Systems Biology

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The adaptive immune response is a complex choreographed interaction of several immune cell types such as T cells, B cells, dendritic cells and mast cells which relies on these cells' ability to recognize self and foreign molecular information and culminates in the activation of a single T cell population. The study of T cell activation remains challenging due to the lack of both an adequate theoretical framework and an experimental methodology for pursuing the dynamic, multi-state, low 'copy number' interactions of a large and growing number of molecular species. The impact of computation and quantitative analysis in T cell biology will not be fully felt until the tools that support these processes have acquired general acceptance in the greater biological, and often computationally disinclined, community.

To this end the Cell Systems Initiative (CSI) has developed BALSA - an integrated toolset to support and enhance both computational and experimental investigations into cell biology which uses a novel symbol set that abstracts the mathematical rigor inherent in creating and executing simulations of reaction networks into linear assemblies of high-level statements of biological phenomena. BALSA, the CAD-style software environment developed at CSI, permits facile authoring with this symbol set via transparent database support, parallel 2D graphical interpretation, and a simple interface for specifying and executing simulations of user-authored models. Simulations are communicated to either SigTran [simulation engine] or the Scooby discrete-event simulation processor using SBML, the Systems Biology Markup Language. SigTran is the powerful modeling engine within BALSA which enables the biological researcher to create, simulate and analyze, on both nonspatial and spatial domains, biochemical reaction or reaction diffusion networks with multistate functionality. SigTran has two major simulation modes – deterministic and stochastic. A reaction system formulated as a system of DAES (Differential Algebraic Equations) or as a kinetic rate based reaction network may be simulated within SigTran in either mode or both modes simultaneously. SigTran has a number of outstanding features including multistate complex and reaction specification which together cannot be found in any other modeling platform. The task of simulating reaction networks as stochastic discrete event processes has been shown to be substantial. The estimated number of reaction events in a whole cell simulation is staggering, despite techniques to compress the dynamic range of reaction processes by approximating the exact solution. Within BALSA a new approach for calculating trajectories for Markov discrete event processes is demonstrated, based on the Scooby discrete-event simulation processor, which performs at least an order of magnitude faster than conventional techniques.